



EL894957885US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

True Applicant(s) : O'Brien, T. J. et al.  
Serial No. : 09/965,738  
Filing Date : September 27, 2001  
Title : REPEAT SEQUENCES OF THE CA125 GENE  
AND THEIR USE FOR DIAGNOSTIC AND  
THERAPEUTIC INTERVENTIONS  
Examiner : Unsigned  
Group Art Unit : 1645

US Patent and Trademark Office  
Attn: Box Missing Parts  
P. O. Box 2327  
Arlington, VA 22202

**TRANSMITTAL OF SUBSTITUTE FORMAL DRAWINGS**

Sir:

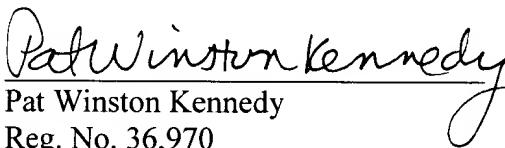
In response to the Notice to File Corrected Application Papers dated November 20, 2001 requesting substitute drawings in compliance with 37 CFR 1.84, Applicants submit herewith substituted formal drawings (FIGS. 1-10) with the requested margin changes incorporated therein.

Kindly direct any other comments or requests with respect to this application to the undersigned Counsel.

No fees are believed to be due since this submission is being filed within the two month response period. However, should a fee be due, the Assistant Commissioner is authorized to charge such fee to Deposit Account No. 16-1435. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

Date: December 4, 2001

  
Pat Winston Kennedy  
Reg. No. 36,970

KILPATRICK STOCKTON LLP  
1001 West Fourth Street  
Winston-Salem, NC 27101  
Phone: (336) 607-7336  
Fax: (336) 607-7500  
**Attorney Docket No.: 40715-260477**  
40715-260477 WINLIB01:920101.1

### Structure of Amino Terminal Domain

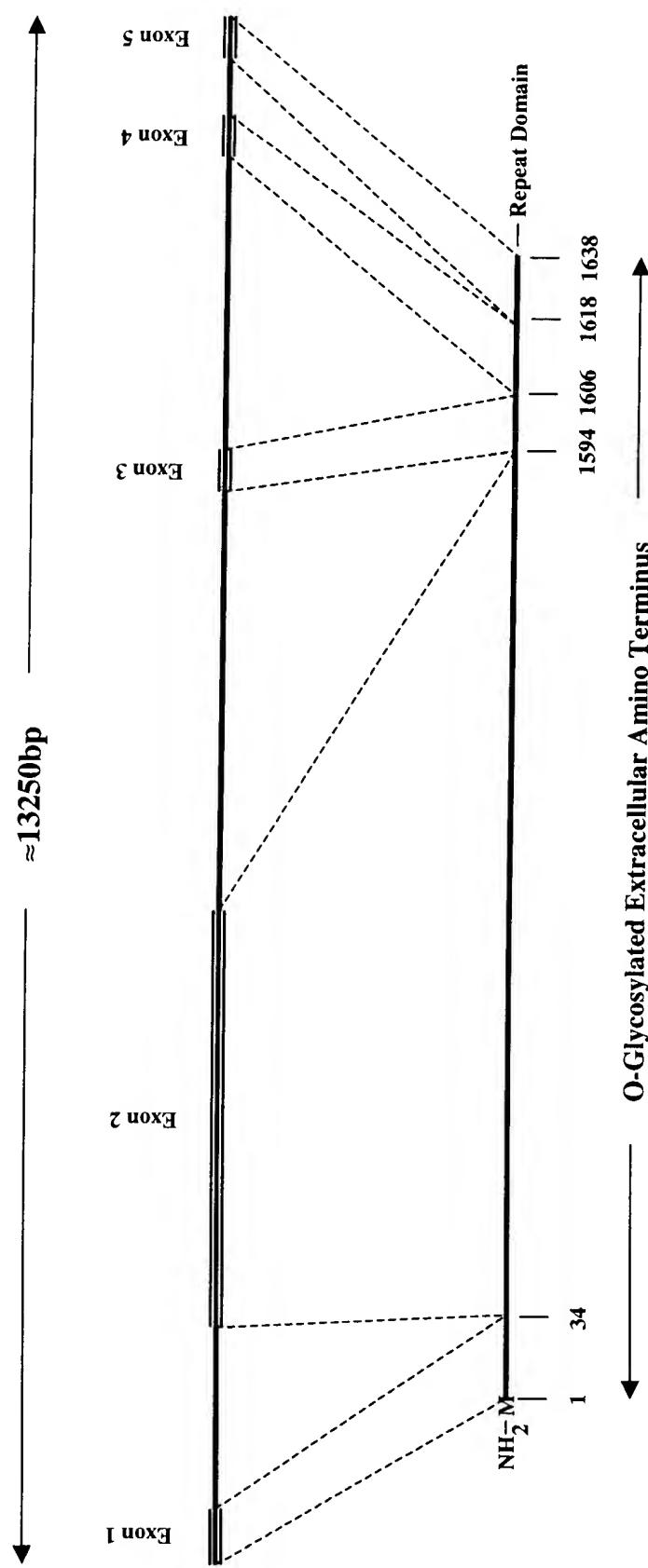


Figure 8A

Figure 8B (SEO ID NO: 299)

## Structure of Carboxy Terminal Domain

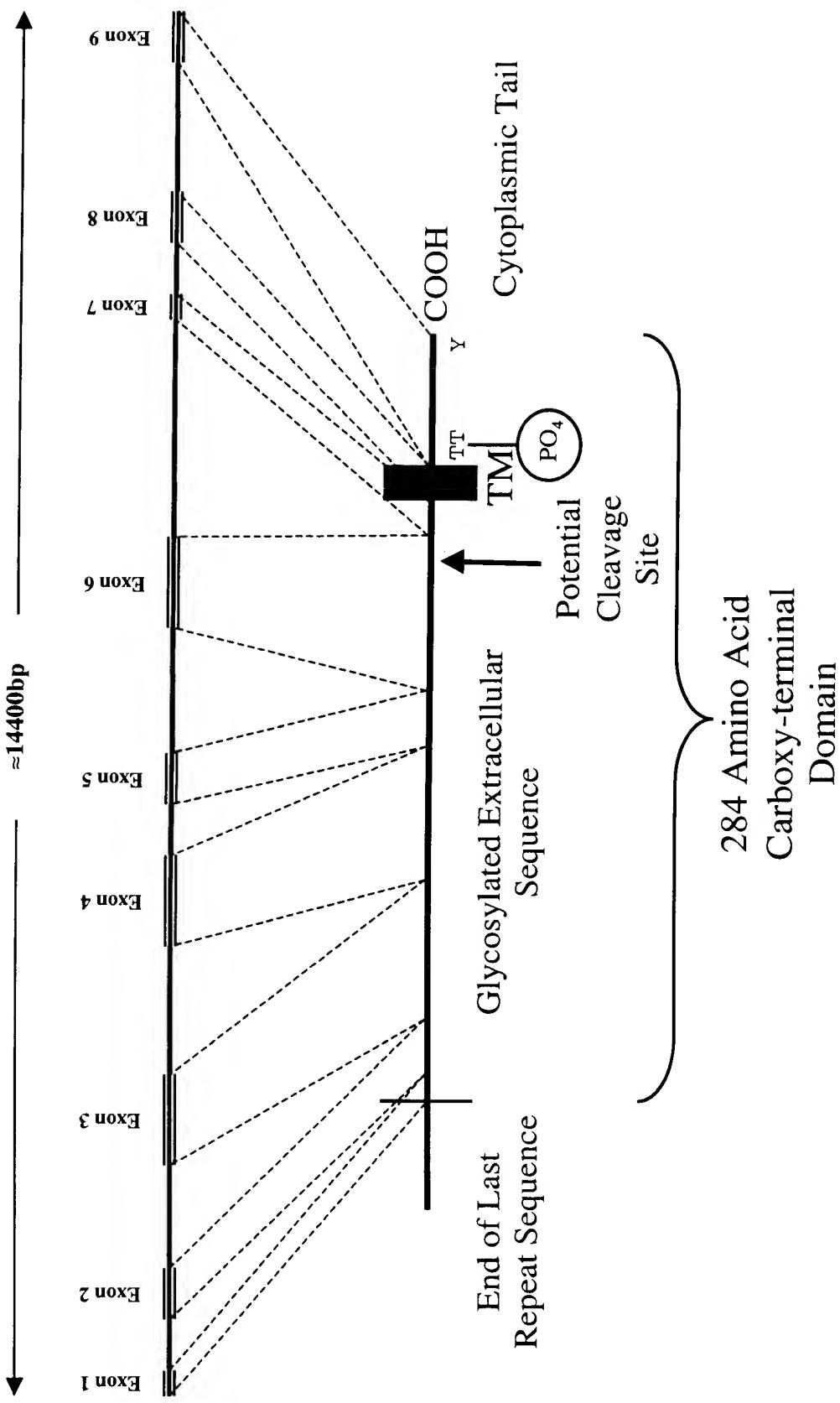


Figure 9A

ITLLRDIQDK VTTLYKGSQL HDTFRFCLVTKT NLTMDSVLVT VKALFSSNLD

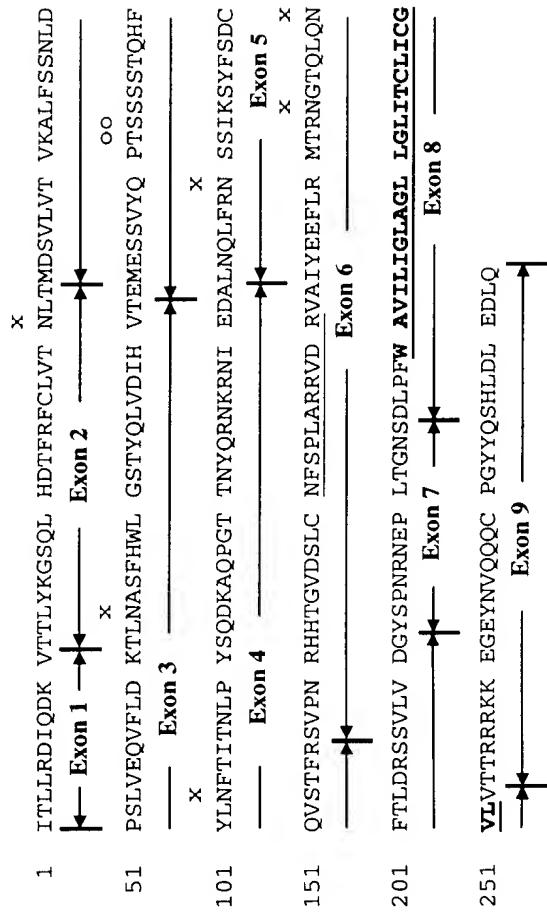


Figure 9B (SEQ ID NO: 300)

## Proposed Structure of CA125

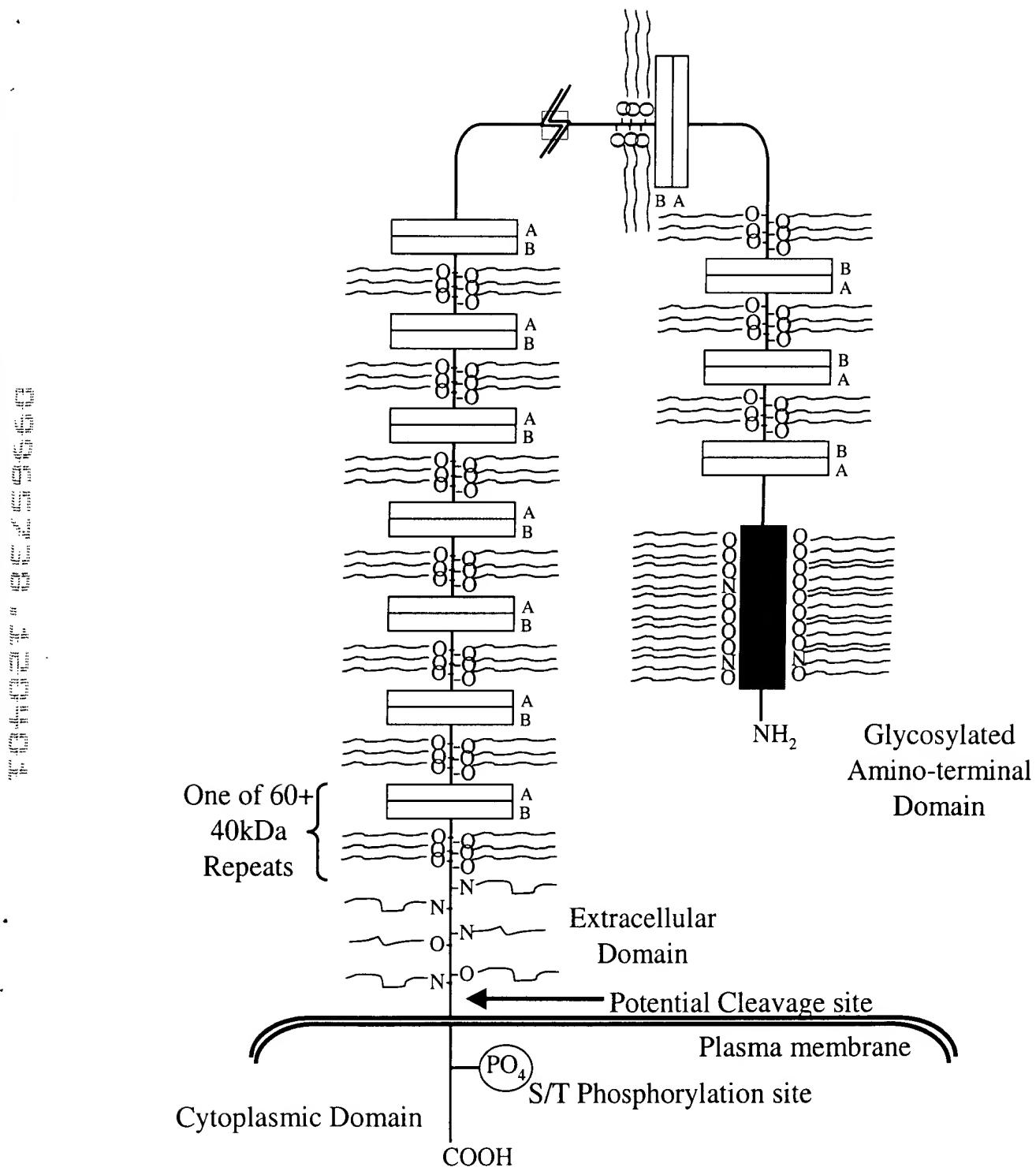


Figure 10

## Cyanogen Bromide (CNBr) Cleavage

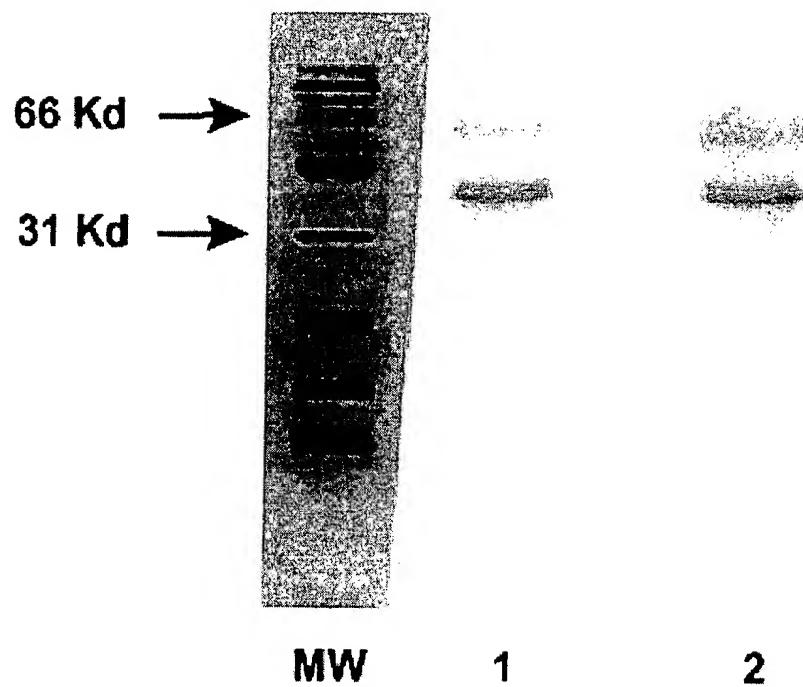
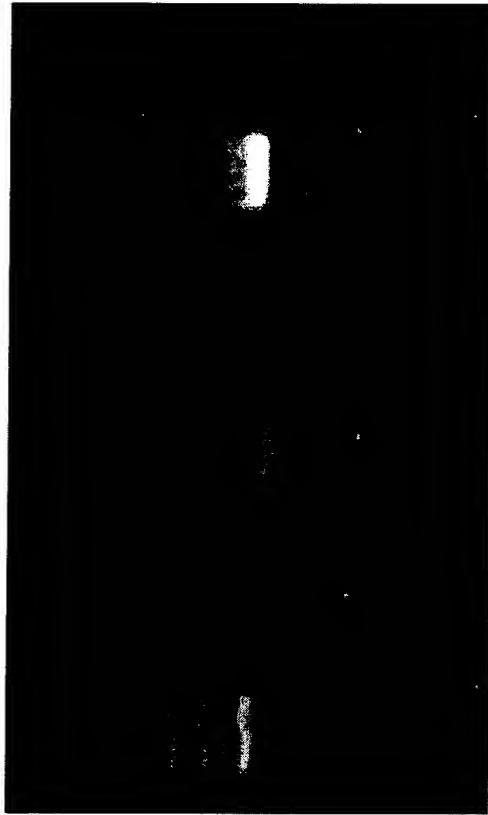


Figure 1

**A**

1 2 3 4 5 6

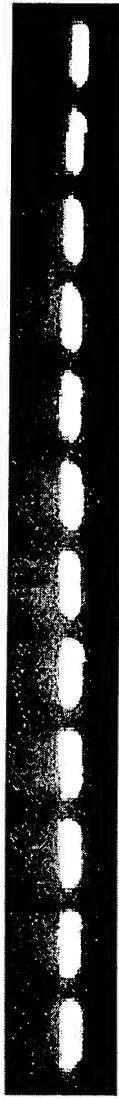
500 bases



**B**

1 2 3 4 5 6 7 8 9 10 11 12

CA125



$\beta$ -Tubulin

Figure 2

# A Strategy for Placing Repeat Sequences in Contiguous Order Using Overlap Sequence Alignment



(SEQ ID NO: 158)

1 ATVPMPVPPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKDSAMAYDAICTHRDPEDLGLDRERLYWELSNLNTGIOELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
156  
157 AACPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKDSAMAYDAICTHRDPEDLGLDRERLYWELSNLNTGIOELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
315 AACPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKDSAMAYDAICTHRDPEDLGLDRERLYWELSNLNTGIOELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
314  
471 TAGPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKDSAMAYDAICTHRDPEDLGLDRERLYWELSNLNTGIOELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
470  
626 AACPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKDSAMAYDAICTHRDPEDLGLDRERLYWELSNLNTGIOELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
625  
781

(SEQ ID NO: 159)

1 SACPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKNGAATGMDAICSHRLDKPSGQLINREPOLYMYLQLNGFTHRSAPVPTSTDGTSSSSPSPIT  
156  
157 TAVPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKNGAATGMDAICSHRLDKPSGQLINREPOLYMYLQLNGFTHRSAPVPTSTDGTSSSSPSPIT  
312  
313 TAGPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKNGAATGMDAICSHRLDKPSGQLINREPOLYMYLQLNGFTHRSAPVPTSTDGTSSSSPSPIT  
468  
469 EOPPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKNGAATGMDAICSHRLDKPSGQLINREPOLYMYLQLNGFTHRSAPVPTSTDGTSSSSPSPIT  
624  
625 EPCPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKNGAATGMDAICSHRLDKPSGQLINREPOLYMYLQLNGFTHRSAPVPTSTDGTSSSSPSPIT  
780

(SEQ ID NO: 159)

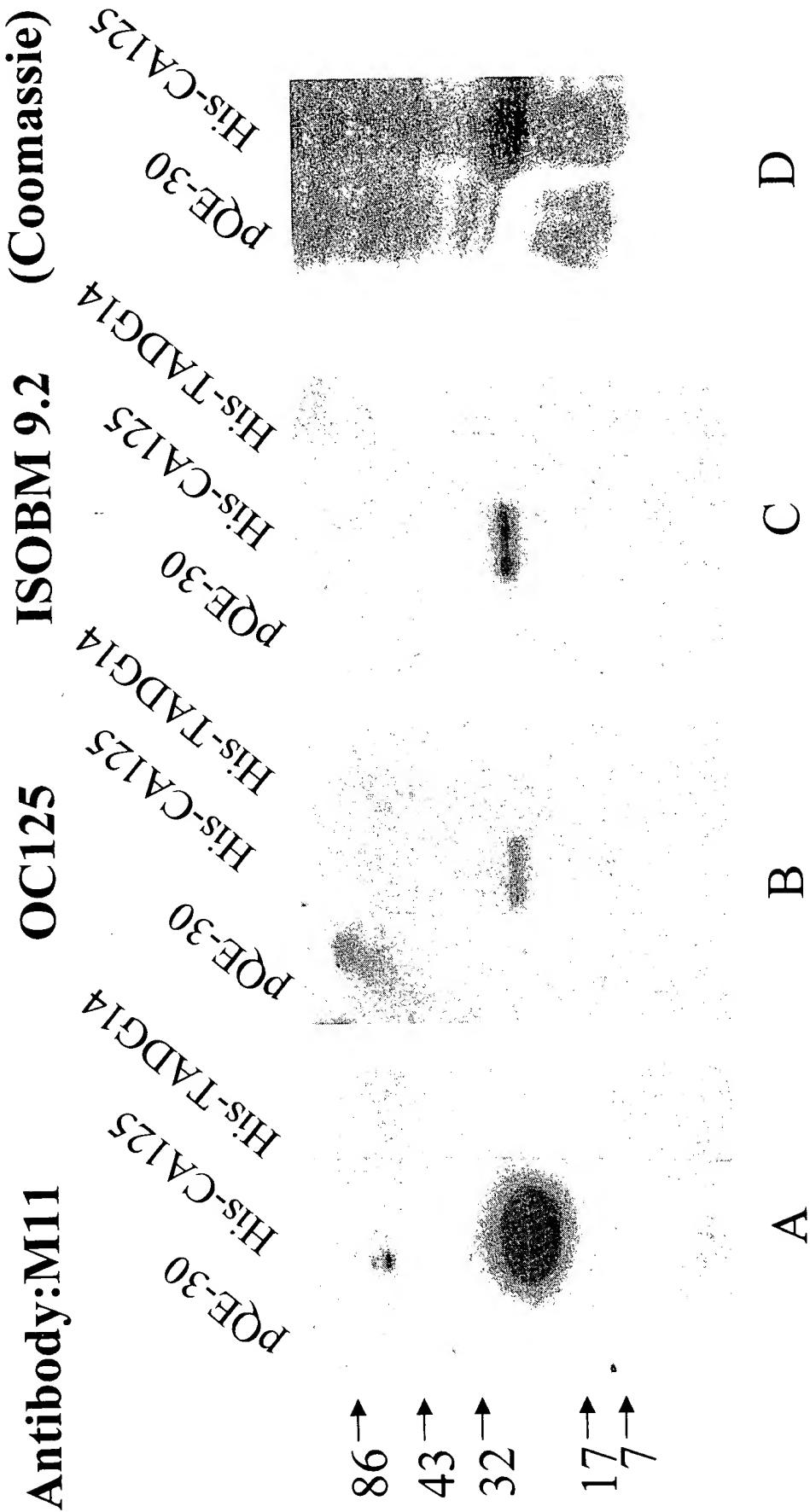
1 TAGPLVLPFTLNFITLNLQYEEDMHRPGSRRFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
156  
157 AVPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
312  
313 ACPPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
468  
469 TASPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
624

(SEQ ID NO: 160)

1 ATGPVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
156  
157 TASPLVLPFTLNFITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
312  
313 AASPLVLPFTLNGTITLNLQYEEDMHRPGSRKFNTTERELQQLKLPLRNSSELEYSGCRLASLRPEKOAATSVDTICTHNDPGLPGLDRERLYWELSOLTSITELGPTYLDRNSLYNGFPHRSMPITSTDGTSSSSPSPIT  
468

Figure 3 (SEQ ID NOS: 158, 159, 160, and 161)

Figure 4



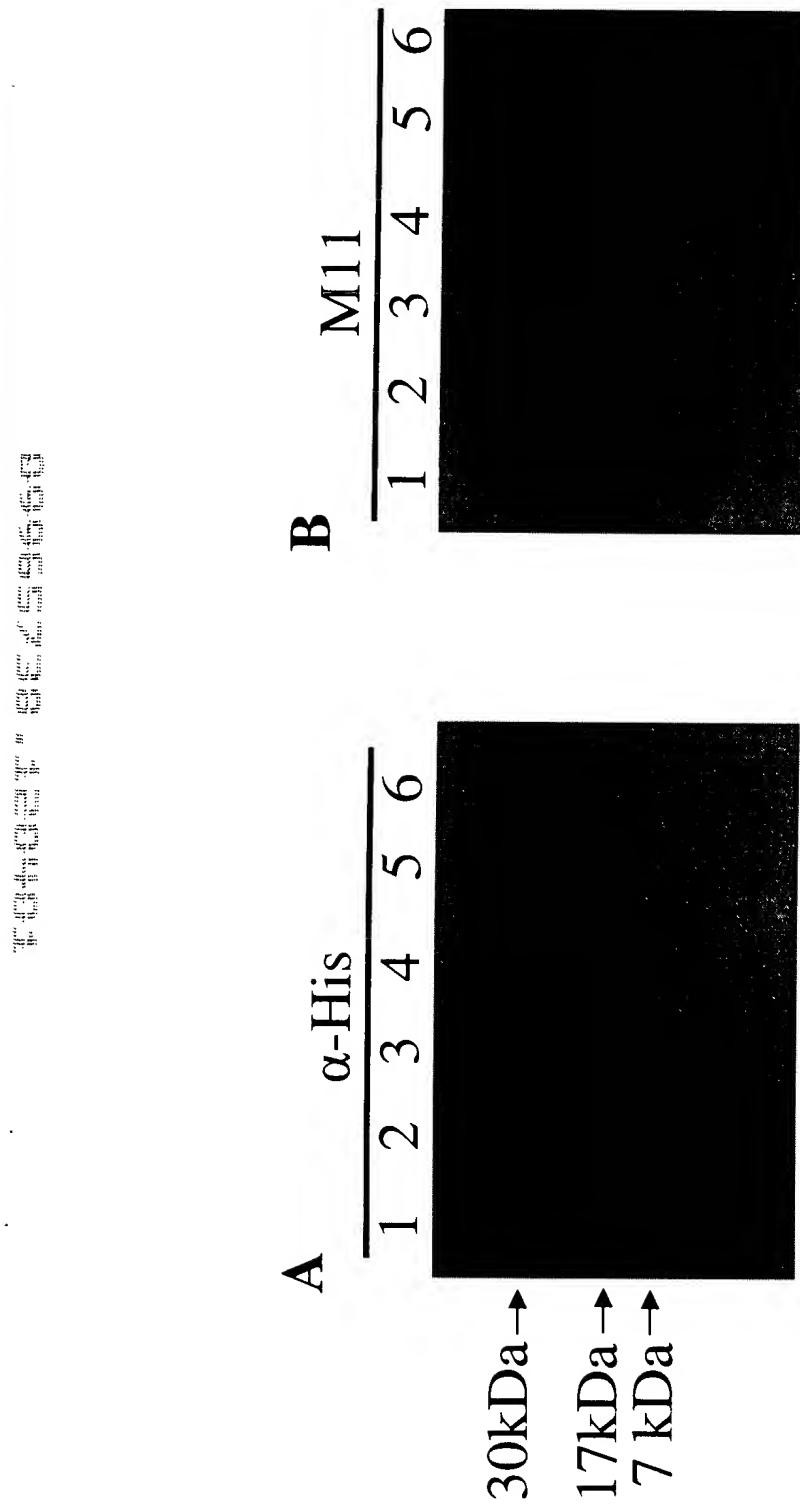
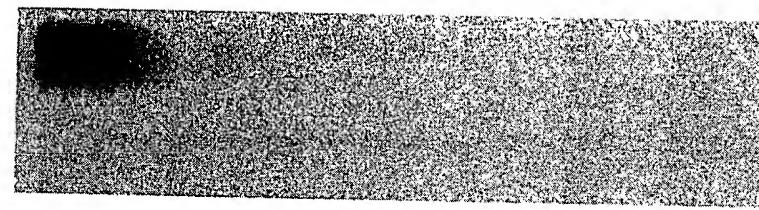


Figure 5 (SEQ ID NO: 150)

9 kb 6 kb 5 kb 3 kb 2 kb 1 kb

N T



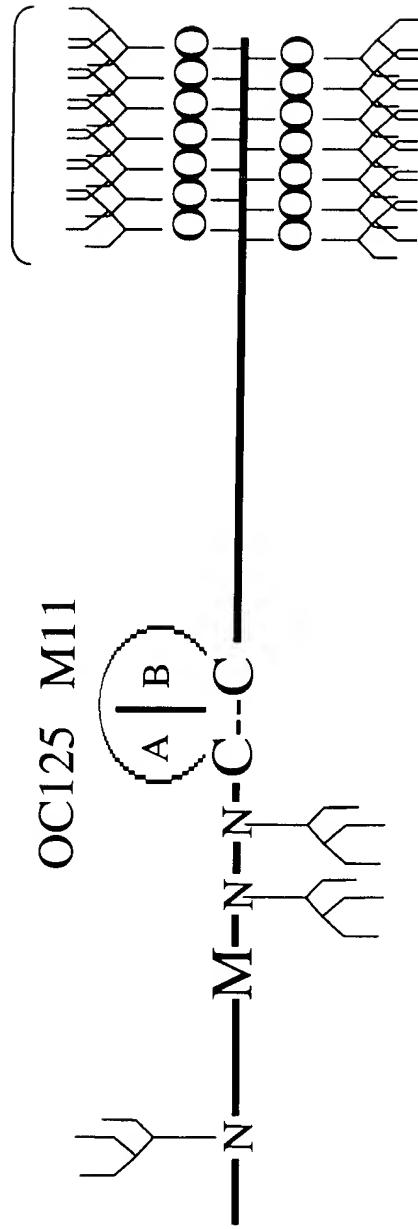
CA125 →

18S



Figure 6

Heavily  
O-glycosylated



156 amino acids  
repeated 60+ times

Figure 7A

Genomic Structure of a 156 Amino Acid Repeat Sequence of CA125

→ ←  $\approx 1900$  bp

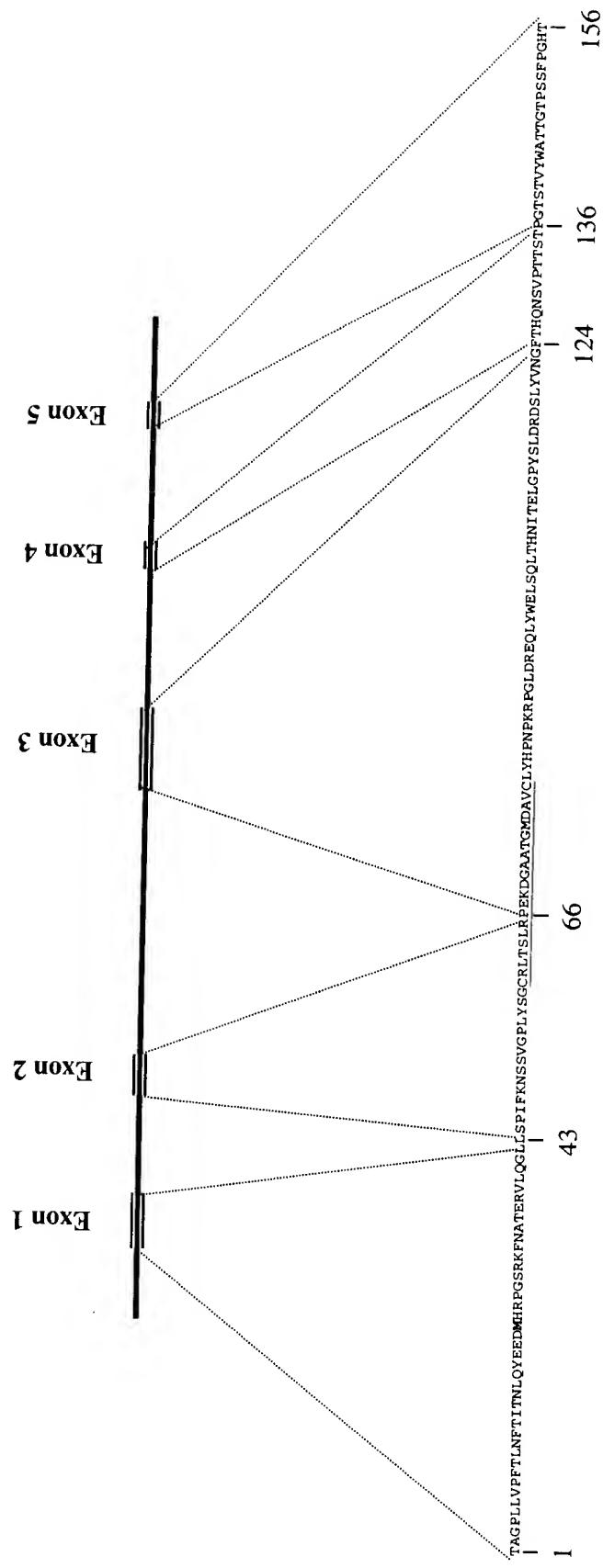


Figure 7B (SEQ ID NO: 163)

### Exon 1

1

42

ATVPPFMVPFTLNFTITNLQYEEDMRHPGSRKFNATEREVLQGL (SEQ ID NO: 164)  
TAVPLLPFTLNFTITNLQYGEDMRHPGSRKFNTTERVLQGL (SEQ ID NO: 165)  
VPGPLLPFTLNFTITNLQYEEAMRHPGSRKFNTTERVLQGL (SEQ ID NO: 166)  
APGPLLPFTLNFTITNLQYEEDMRHPGSRKFNTTERVLQGL (SEQ ID NO: 167)  
APGPLLPFTLNFTITNLQYEEDMRHPGSRKFNTTERVLQGL (SEQ ID NO: 168)  
APGPLLPFTLNFTITNLQYEVDMRHPGSRKFNTTERVLQGL (SEQ ID NO: 169)  
SAGPLLPFTLNFTITNLQYEEDMRHPGSRKFNTTERVLQGL (SEQ ID NO: 170)  
AAGPLLMPTLNFTITNLQYEEDMRRTGSRKFNNTMESVLQGL (SEQ ID NO: 171)  
TASPLLVLFITINCTITNLQYEEDMRRTGSRKFNNTMESVLQGL (SEQ ID NO: 172)  
AAGPLLPFTLNFTITNLQYGEDMGHHPGSRKFNTTERVLQGL (SEQ ID NO: 173)  
TAGPLLIPTLNFTITNLQYGEDMGHHPGSRKFNTTERVLQGL (SEQ ID NO: 174)  
TAGPLLPFTLNFTITNLQYGEDMGHHPGSRKFNTTERVLQGL (SEQ ID NO: 175)  
TAGPLLVLFITLNFTITNLKYEEDMHRPGSRKFNTTERVLQTL (SEQ ID NO: 176)  
TAGPLLPFTLNFTITNLQYEEDMHRPGSRKFNATERVLQGL (SEQ ID NO: 177)  
TAGPLLPFTLNFTITNLQYEEDMHRPGSRKFNTTERVLQGL (SEQ ID NO: 178)  
TAGPLLPFTLNFTITNLQYEEDMHRPGSRKFNTTERVLQGL (SEQ ID NO: 179)  
APVPLLIPTLNFTITNLQYEEDMHRPGSRKFNTTERVLQGL (SEQ ID NO: 180)  
ATGPVLLPFTLNFTITNLQYEEDMHRPGSRKFNTTERVLQGL (SEQ ID NO: 181)  
AAGPLLVLPFTLNFTITNLQYEEDMHHPGSRKFNTTERVLQGL (SEQ ID NO: 182)  
SAGPLLPFTLNFTITNLQYEEDMHHPGSRKFNTTERVLQGL (SEQ ID NO: 183)  
TASPLLVLFITNFTITNQRYEENMHHPGSRKFNTTERVLQGL (SEQ ID NO: 184)  
TASPLLVLFITNFTITNLRYEENMHHPGSRKFNTTERVLQGL (SEQ ID NO: 185)  
EPGPLLIPTFNFTITNLHYEENMQHPGSRKFNTTERVLQGL (SEQ ID NO: 186)  
EPGPLLIPTFNFTITNLRYEENMQHPGSRKFNTTERVLQGL (SEQ ID NO: 187)  
APVPLLIPTLNFTITNLHYEENMQHPGSRKFNTTERVLQGL (SEQ ID NO: 188)  
APVPLLIPTLNFTITDLHYEENMQHPGSRKFNTTERVLQGL (SEQ ID NO: 189)  
AASPLLVLFITNFTITNLRYEENMQHPGSRKFNTTERVLQGL (SEQ ID NO: 190)  
TAGPLLPFTLNFTITNLKYEEDMHCPGSRKFNTTERVLQSL (SEQ ID NO: 191)  
AASHLLILFTLNFTITNLRYEENMW.PGSRKFNTTERVLQGL (SEQ ID NO: 192)  
TGVVSEEPFTLNFTITNLLRYMADMGQPGSLKFNITDNVMKHL (SEQ ID NO: 193)  
AMGYHLKTLTNFTISNLQYSPDMGKGSATFNSTEGVLQHLL (SEQ ID NO: 194)

Figure 7C

**Exon 2**

43	65
LKPLFRNSSLEYLYSGCRLASLR	(SEQ ID NO: 195)
LKPLFKNTSVSSLYSGCRLTLLR	(SEQ ID NO: 196)
LKPLFKNTSVGPLYSGCRLTLLR	(SEQ ID NO: 197)
LKPLFKSTSVGPLYSGCRLTLLR	(SEQ ID NO: 198)
LKPLFKSTSVGPLYSSCRLTLLR	(SEQ ID NO: 199)
LKPLFKNTSVGPLYSGCRLTSLR	(SEQ ID NO: 200)
LGPIFKNTSVGPLYSGCRLTSLR	(SEQ ID NO: 201)
LGPMFKNTSVGLLYSGCRLTLLR	(SEQ ID NO: 202)
LGPMFKNTSVGPLYSGCRLTLLR	(SEQ ID NO: 203)
LGPMFKNTSVGPLYSGCRLTSLR	(SEQ ID NO: 204)
LGPLFKNNSVGPLYSGCRLISLR	(SEQ ID NO: 205)
LGPLFKNNSVDPPLYSGCRLTSLR	(SEQ ID NO: 206)
LSPIFKNSSVGPLYSGCRLTSLR	(SEQ ID NO: 207)
LSPIFKNTSVGPLYSGCRLTLLR	(SEQ ID NO: 208)
LSPLFQRSSLGARYTGCRVIALR	(SEQ ID NO: 209)
LRPLFKNTSVSSLYSGCRLTLLR	(SEQ ID NO: 210)
LRPLFKNTSVGPLYSGSRLTLLR	(SEQ ID NO: 211)
LRPLFKNTSIGPLYSSCRLTLLR	(SEQ ID NO: 212)
LRPLFKSTSVGPLYSGCRLTLLR	(SEQ ID NO: 213)
LRPVFKNTSVGLLYSGCRLTLLR	(SEQ ID NO: 214)
LRPVFKNTSVGPLYSGCRLTLLR	(SEQ ID NO: 215)
LRSLFKSTSVGPLYSGCRLTLLR	(SEQ ID NO: 216)
LRSLFKSTSVGPLYSGCRLTSLR	(SEQ ID NO: 217)
LTPLFKNTSVGPLYSGCRLTLLR	(SEQ ID NO: 218)
LTPLFRNTSVSSLYSGCRLTLLR	(SEQ ID NO: 219)
LMPLFKNTSVSSLYSGCRLTLLR	(SEQ ID NO: 220)
RPLFQKSSM.GPFYLGQQLISLR	(SEQ ID NO: 221)

**Figure 7C**

### Exon 3

66

123

PEKDSSAMAVDAICTHRPDPEDLGLDRERLYWELSNLTNGIQELGPYTLDRNSLYVNG (SEQ ID NO: 222)  
PEKDGAATGVDAICTHRLDPKSPGLNREQLYWELSKLTNDIEELGPYTLDRNSLYVNG (SEQ ID NO: 223)  
PKKDGAATGVDAICTHRLDPKSPGLNREQLYWELSKLTNDIEELGPYTLDRNSLYVNG (SEQ ID NO: 224)  
PEKDGTATGVDAICTHHPDPKSPRLDREQLYWELSQLTHTNITELGHYALDNDSLFVNG (SEQ ID NO: 225)  
PEKDGEATGVDAICTHRPDPGPGLDREQLYLELSQLTHSITELGPYTLDRDSLYVNG (SEQ ID NO: 226)  
PEKDGAATGMDAVCLYHPNPKRPGLDREQLYWELSQLTHTNITELGPYSLDRDSLYVNG (SEQ ID NO: 227)  
PEKDGAATGMDAVCLYHPNPKRPGLDREQLYCELSQLTHTNITELGPYSLDRDSLYVNG (SEQ ID NO: 228)  
PEKDGAATRVDAACTYRPDPKSPGLDREQLYWELSQLTHTSITELGPYTLDRVSLYVNG (SEQ ID NO: 229)  
PKKDGAATKVAICTYRPDPKSPGLDREQLYWELSQLTHTSITELGPYQDRDSLYVNG (SEQ ID NO: 230)  
PKKDGAATKVAICTYRPDPKSPGLDREQLYWELSQLTHTSITELGPYQDRDSLYVNG (SEQ ID NO: 231)  
PEKDGAATRVDAVCTHRPDPKSPGLDRERLYWKLSQLTHTGITELGPyTLDRHSLYVNG (SEQ ID NO: 232)  
PEKDGVATRVDAICTHRPDPKIPGLDRQQLYWELSQLTHTSITELGPYTLDRDSLYVNG (SEQ ID NO: 233)  
SEKDGAATGVDAICCIHHLDPKSPGLNRERLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 234)  
SEKDGAATGVDAICTHRLDPKSPGLDREQLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 235)  
SEKDGAATGVDAICTHRLDPKSPGVDRQQLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 236)  
SEKDGAATGVDAICTHRVDPKSPGVDRQQLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 237)  
SEKDGAATGVDAICTHHLNPQSPGLDREQLYWQLSQMTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 238)  
PEKRGAATGVDTICTHRLDPLNPGLDREQLYWELSKLTRGIIELGPYLLDRGSLYVNG (SEQ ID NO: 239)  
PEKNGAATGMADAICSHRLDPKSPGLNREQLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 240)  
PEKNGAATGMADAICSHRLDPKSPGLDREQLYWELSQLTNGIKELGPYTLDRNSLYVNG (SEQ ID NO: 241)  
PEKHGAATGVDAICTLRLDPTGPGLDRERLYWELSQLTNSITELGPyTLDRDSLYVNG (SEQ ID NO: 242)  
PEKHGAATGVDAICTLRLDPTGPGLDRERLYWELSQLTNSITELGPyTLDRDSLYVNG (SEQ ID NO: 243)  
PEKHEAATGVDTICTHRVDPIGPGLDRERLYWELSQLTNSITELGPyTLDRDSLYVNG (SEQ ID NO: 244)  
PEKQEAATGVDTICTHRVDPIGPGLDRERLYWELSQLTNSITELGPyTLDRDSLYVNG (SEQ ID NO: 245)  
PEKQEAATGVDTICTHRVDPIGPGLDRERLYWELSQLTNSITELGPyTLDRDSLYVNG (SEQ ID NO: 246)  
PEKDKAATRVDAICTHHPDPQSPGLNREQLYWELSQLTNGIKELGPYTLDRDSLYVNG (SEQ ID NO: 247)  
SVKNGAETRVDLLCTYLQPLSGPGLPIKQVFHELSQQTHGIRLGPYSLDKDSLNG (SEQ ID NO: 248)  
PEKDGAATGVDTCTYHPDPVGPGLDIQQLYWELSQLTHTGVTQLGFYVLDRLDSLFING (SEQ ID NO: 249)

Figure 7C

<b>Exon 4</b>		<b>Exon 5</b>
124	135	136
FTHRSSMPTTST (SEQ ID NO: 250)		PGTSTVDVGTSGTPSSSPSPT (SEQ ID NO: 278)
FTHRSSMPTTSI (SEQ ID NO: 251)		PGTSTVDLRTSGTPSSLSSPTIM (SEQ ID NO: 279)
FTHRTSVPTSST (SEQ ID NO: 252)		PGTSTVDLGTSGTPFSLPSPA (SEQ ID NO: 280)
FTHRTSVPTTST (SEQ ID NO: 253)		PGTSTVDLG.SGTPSSLPSPT (SEQ ID NO: 281)
FTHRSSVPTTSS (SEQ ID NO: 254)		PGTSTVDLG.SGTPSPLPSPT (SEQ ID NO: 282)
FTHRSSVSTTST (SEQ ID NO: 255)		PGTSTVDLGTSGTPSSLPSPT (SEQ ID NO: 283)
FTHRSSVAPTTST (SEQ ID NO: 256)		PGTPTVDLGTSGTPVSKPGPS (SEQ ID NO: 284)
FTHRSSGLTTST (SEQ ID NO: 257)		PWTSTVDLGTSGTPSPVPSPPT (SEQ ID NO: 285)
FTHRSFGLTTST (SEQ ID NO: 258)		PGTSTVYWATTGTPSSFPGHT (SEQ ID NO: 286)
FTHRSSFLTTST (SEQ ID NO: 259)		PGTSTVHLATSGTPSSLPGHT (SEQ ID NO: 287)
FTHRNFVPITST (SEQ ID NO: 260)		PGTSTVHLATSGTPSPLPGHT (SEQ ID NO: 288)
FTHRSSVPTTSI (SEQ ID NO: 261)		PDTSTMHLATSRTPASLSGPT (SEQ ID NO: 289)
FTHQSSVSTTST (SEQ ID NO: 262)		PGTSAVHLATSGTPSSLPGHT (SEQ ID NO: 290)
FTHQTSAPNTST (SEQ ID NO: 263)		PGTSAVHLATTGTPSSFPGHT (SEQ ID NO: 291)
FTHQTFAPNTST (SEQ ID NO: 264)		PGTSTVHLGTSETPSSLPRPI (SEQ ID NO: 292)
FTHQNSVPTTST (SEQ ID NO: 265)		PGTSIVNLGTSGIPPSLPETT (SEQ ID NO: 293)
FTHQSSMTTTRT (SEQ ID NO: 266)		PGTFTVQPETSETPSSLPGPT (SEQ ID NO: 294)
FTHWIPVPTSST (SEQ ID NO: 267)		PGTPTVDLGTSGTPVSKPGPS (SEQ ID NO: 295)
FTHWSPIPTTST (SEQ ID NO: 268)		PGTPTVYLGASKTPASIFGPS (SEQ ID NO: 296)
FTHWSSGLTTST (SEQ ID NO: 269)		PKPATTFLLPPLSEATT..... (SEQ ID NO: 297)
FHPRSSVPTTST (SEQ ID NO: 270)		QINFHIVNWNLNSNPDPTSSEY (SEQ ID NO: 298)
FNP RSSVPTTST (SEQ ID NO: 271)		
FNPWSSVPTTST (SEQ ID NO: 272)		
FTQRSSVPTTSI (SEQ ID NO: 273)		
FTQRSSVPTTST (SEQ ID NO: 274)		
FTQRSSVPTTSV (SEQ ID NO: 275)		
YNEPGLDEPPTT (SEQ ID NO: 276)		
YAPQNLISRGEY (SEQ ID NO: 277)		

**Figure 7C**